REMARKS

Claims 9-12 and 14-23 are pending in the present application and are rejected. Claims 9-12 and 17-20 are herein amended. No new matter has been added.

Applicants' Response to Claim Objections

The Office Action indicates that claims 9 and 17 are objected to due to two informalities. First, the Office Action states that the phrase "osteo-induc*ible* transcription factor Cbfa1" should instead be written as "osteo-induc*ing* transcription factor Cbfa1." The Office Action states that this is because "osteo-inducible" implies that the Cbfa1 is induced by "osteo," while "osteo-inducing" means that the Cbfa1 induces "osteo" genes. Applicants herein adopt this proposed amendment.

Additionally, the Office Action states that the phrase "vector *carrying* a gene encoding" as recited in claims 9 and 17, would be more precise if written as "vector *comprising* a gene encoding." Applicants herein adopt this proposed amendment. Additionally, Applicants herein amend the claims to correct the characters in the claims from "ß-TCP" to "β-TCP." No new matter has been added.

Applicants' Response to Claim Rejections under 35 U.S.C. §102

Claims 9-12 and 14-23 were rejected under 35 U.S.C. §102(a) and 102(e) as being anticipated by Doll et al. (U.S. Patent Application Publication No. 2003/0235564), as evidenced by Ogawa et al (U.S. Patent No. 5,030,611).

It is the position of the Office Action that Doll discloses the embodiments as claimed. Doll is directed at compositions and devices comprising the Runx2 protein. Doll discloses using either the Runx2 protein itself, a polynucleotide encoding the Runx2 protein, or a cell that has been transformed with a polynucleotide encoding the Runx2 protein. Paragraph [0010]. Doll discloses the use of retroviral and adenoviral vectors at paragraph [0096]-[0098]. The Office Action states that paragraph [0053] discloses the use of β-TCP. Although paragraph [0053] does not appear to disclose this, paragraphs [0052], [0055], [0056], and [0086] appear to disclose the use of tricalcium phosphates.

As to adsorption, the Office Action states that "[t]he inherent properties of β-TCP to adsorb nucleic acids and/or proteins are known in the art. For instance, Ogawa et al. teaches packing tricalcium phosphate (TCP) or hydroxyapatite for chromatography, and TCP exhibits a high ability to adsorb acidic proteins and nucleic acid." See page 6, second paragraph of June 20, 2008 Office Action. The Office Action cites to column 4, lines 28-33 and column 4, lines 54-59 of Ogawa.

Ogawa is directed at a porous ceramics material which appears to be intended for use in chromatography procedures. Ogawa contemplates ceramics materials including hydroxyapatite and tricalcium phosphate. Ogawa states that hydroxyapatite can be used for packing for

chromatography for "separating and purifying various biomaterials such as proteins, enzymes, nucleic acids, etc." Column 4, lines 28-33. Ogawa further states that the combination of hydroxyapatite and tricalcium phosphate can be used for packing for chromatography and "exhibits a high ability to adsorb acidic proteins." Column 4, lines 54-59. However, Ogawa only mentions that its ceramics materials can adsorb acidic proteins. As an example of this, Ogawa identifies bovine serum albumin (BSA). Column 1, lines 51-54. Ogawa does NOT identify a ceramics material which adsorbs nucleic acids.

In response, Applicants first respectfully submit that Ogawa does not disclose the subject matter alleged by the Office Action. The Office Action states that Ogawa discloses a material which can "adsorb acidic proteins and nucleic acid." Page 6, second paragraph of June 20, 2008 Office Action. However, Ogawa does NOT identify any material which adsorbs nucleic acids. While Ogawa may refer to the use of hydroxyapatite and tricalcium phosphate to separate and purify nucleic acids, Ogawa does not state that anything other than acidic proteins will be adsorbed on the bioadaptable porous materials. Furthermore, Applicants note that the adsorption of protein is irrelevant to the claims. The claims require that a vector comprising a gene encoding Cbfa1 is adsorbed onto bioadaptable porous material. The claims do not address a protein being adsorbed onto bioadaptable porous material.

Additionally, Applicants respectfully submit that even if, *arguendo*, Ogawa did disclose the adsorption of nucleic acids onto biomaterials in addition to adsorption of acidic proteins onto biomaterials, such alleged adsorption would not be an inherent property of hydroxyapatite or β-TCP. Rather, this alleged adsorption is dependent on the manner in which the ceramics material

is produced. For example, Ogawa identifies another method of producing hydroxyapatite, in which "disadvantageously the ability of the treated particles to adsorb acidic proteins such as bovine serum albumin (BSA) is lowered." Column 1, lines 52-54. As such, even if, *arguendo*, Ogawa disclosed or suggested adsorption of nucleic acids onto a bioadaptable material, it can be presumed that such adsorption would also depend on the method of manufacture of the bioadaptable material. According to MPEP § 2112:

> In relying upon the theory of inherency, the examiner must provide a basis in fact and/or technical reasoning to reasonably support the determination that the allegedly inherent characteristic necessarily flows from the teachings of the applied prior art. *Ex parte Levy*, 17 USPQ2d 1461, 1464 (emphasis in original).
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> To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill. Inherency, however, may not be established by probabilities or possibilities. The mere fact that a certain thing *may* result from a given set of circumstances is not sufficient.' *In re Robertson*, 169 F.3d 743, 745, 49 USPQ2d 1949, 1950-51 (Fed. Cir. 1999) (citations omitted) (emphasis added).

In other words, in order to rely on the argument that Doll inherently discloses the claimed subject matter, it must be shown that adsorption of a vector comprising the Cbfa1 gene onto the bioadaptable material of Doll necessarily occurs. As explained above, adsorption of biomaterials does not necessarily occur in a bioadaptable material made of hydroxyapatite or tricalcium phosphate. Rather, the ability of a bioadaptable material made of hydroxyapatite or tricalcium phosphate to adsorb biomaterials is at least partially dependent on its method of manufacture. As such, the mere fact that a bioadaptable porous material of hydroxyapatite or tricalcium phosphate made by a particular procedure discussed in Ogawa *may* adsorb biomaterials such as acidic

proteins, is not sufficient to show that this adsorption is an inherent characteristic of the bioadaptable materials of Doll, particularly in view of the fact that Doll is silent as to the method of manufacturing its bioadaptable porous material.

Furthermore, even if, *arguendo*, Ogawa suggested the affinity of β-TCP to proteins and nucleic acids, it is difficult for proteins or nucleic acids to be efficiently adsorbed to a porous β-TCP by the method described in Doll, irrespective of the method of manufacture of the bioadaptable porous materials. The adsorption efficacy of β-TCP to proteins or nucleic acids is very low when β-TCP is merely mixed with a solution comprising proteins or nucleic acids. The reason is that a porous β-TCP is a very light material and does not sink down into a solution when it is placed in the solution. Additionally, a solution can hardly penetrate into this material because the surface of the material is relatively water repellant. Doll is silent as to the conditions under which Runx2 is incorporated into the bioadaptable porous material. However, a low pressure condition as used in the specification overcomes such problems and allows cells, proteins or viruses penetrating into a porous β-TCP to directly contact with the surface of the material. Thereby, adsorption can successfully occur. Doll does not disclose the use of this low-pressure condition.

In other words, the ability of the bioadaptable material to adsorb a biomaterial is not only based on the method of manufacture of the bioadaptable material, but is also based on the conditions under which the biomaterial is incorporated into the bioadaptable material. A lower pressure environment, such that used in the present application, will give rise to adsorption. However, examples of conditions which give rise to non-adsorption include: (i) a high-pressure

environment, (ii) immobilization (crosslinking) of genes to the implant by UV irradiation, and (iii) mixing bioadaptable filling such as collagen gel and alginate with genes to make an implant.

Additionally, it is noted that the Office Action states that "the claims do not recite any specific condition (low pressure, degasified, for instance) how adsorption occurs." However, Applicants respectfully submit that the pending claims are apparatus claims, not method claims or product-by-process claims. As such, it is not necessary to recite specific conditions. The claims read on an implant having Runx2 adsorbed onto a bioadaptable material, regardless of how this adsorption occurred. Applicants' previous remarks were merely illustrative of the point that a nucleic acid may or may not be adsorbed on an implant, depending in part on the conditions of incorporation. As such, it is improper to presume that any reference which cites Runx2 and bioadaptable materials, such as Doll, anticipates the claim.

In summary, Applicants respectfully submit:

1. Ogawa does not disclose adsorption of nucleic acids on to a bioadaptable material, but rather only discloses adsorption of acidic proteins onto a bioadaptable material.

2. Ogawa discloses that the ability of a bioadaptable material to adsorb acidic proteins depends upon the method of manufacture of the bioadaptable material. Even if Ogawa disclosed or suggested adsorption of nucleic acids onto a bioadaptable material, it can be presumed that such adsorption would also depend on the method of manufacture of the bioadaptable material.

3. The ability of a bioadaptable material to adsorb nucleic acids also depends upon the conditions of incorporation.

In view of the above, Applicants respectfully submit that Doll does not inherently or explicitly disclose a bioadaptable porous material on which nucleic acids are adsorbed, and that adsorption of biomaterials, such as nucleic acids and acidic proteins, is not an inherent feature of

a bioadaptable porous material. In fact, there are two stages of uncertainty: (i) the method of manufacture of the bioadaptable porous material and (ii) the method of incorporation of the biomaterial on the bioadaptable porous material. Additionally, Applicants draw the Examiner's attention to the enclosed Declaration under 37 CFR 1.132 where the above points are also attested to by one of the inventors in the pending application. Therefore, for at least the above reasons, Applicants respectfully submit that Doll does not explicitly or inherently disclose or suggest the embodiments as claimed. Favorable reconsideration is respectfully requested.

For at least the foregoing reasons, the claimed invention distinguishes over the cited art and defines patentable subject matter. Favorable reconsideration is earnestly solicited.

Should the Examiner deem that any further action by applicants would be desirable to place the application in condition for allowance, the Examiner is encouraged to telephone applicants' undersigned attorney.

If this paper is not timely filed, Applicants respectfully petition for an appropriate extension of time. The fees for such an extension or any other fees that may be due with respect to this paper may be charged to Deposit Account No. 50-2866.

Respectfully submitted,

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Enclosure: Declaration under 37 CFR 1.132